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1: Curr Biol. 1996 Dec 1;6(12):1669-76.

Apo-3, a new member of the tumor necrosis factor receptor family, contains a death domain and activates apoptosis and NF- κ B.

Marsters SA, Sheridan JP, Donahue CJ, Pitti RM, Gray CL, Goddard AD, Bauer KD, Ashkenazi A.

Department of Molecular Oncology, Genentech, Inc., South San Francisco, California 94080-4918, USA.

BACKGROUND: Two receptors that contain the so-called "death domain" have been described to date: tumor necrosis factor receptor 1 (TNFR1) and Fas/Apo-1 (CD95); both belong to the TNFR gene family. The death domain of TNFR1 mediates the activation of programmed cell death (apoptosis) and of the transcription factor NF- κ B, whereas the death domain of CD95 only appears to activate apoptosis. **RESULTS:** We have identified an additional member of the TNFR family, which we have named Apo-3. Apo-3 is a transmembrane protein of approximately 47 kDa that has similarity of members of the TNFR family in its extracellular, cysteine-rich domains. In addition, Apo-3 resembles TNFR1 and CD95 in that it contains a cytoplasmic death domain. The Apo-3 gene mapped to human chromosome 1p36.3, and Apo-3 mRNA was detected in several human tissues, including spleen, thymus, peripheral blood lymphocytes, small intestine and colon. Ectopic expression of Apo-3 in HEK293 or HeLa cells induced marked apoptosis. CrmA, a poxvirus inhibitor of Ced-3-like proteases which blocks death signaling by TNFR1 and CD95, inhibited Apo-3-induced apoptosis. Ectopic expression of Apo-3 also induced the activation of NF- κ B. Apo-3 did not specifically bind to the Apo-2 ligand, suggesting the existence of a distinct ligand for Apo-3.

CONCLUSIONS: These results identify Apo-3 as a third member of the TNFR family that activates apoptosis, and suggest that Apo-3, TNFR1 and CD95 engage a common apoptotic cell-death machinery. Apo-3 resembles TNFR1 because it can stimulate NF- κ B activity and regulate apoptosis. Apo-3 mRNA is expressed in various tissues, consistent with the possibility that this receptor may regulate multiple signaling functions.



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1: Curr Biol. 1997 Dec 1;7(12):1003-6.

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A novel receptor for Apo2L/TRAIL contains a truncated death domain.

Marsters SA, Sheridan JP, Pitti RM, Huang A, Skubatch M, Baldwin D, Yuan J, Gurney A, Goddard AD, Godowski P, Ashkenazi A.

Department of Molecular Oncology, Genentech Inc., 1 DNA Way, South San Francisco, California 94080-4918, USA.

Apo2 ligand (Apo2L [1], also called TRAIL for tumor necrosis factor (TNF)-related apoptosis-inducing ligand [2]) belongs to the TNF family and activates apoptosis in tumor cells. Three closely related receptors bind Apo2L: DR4 and DR5, which contain cytoplasmic death domains and signal apoptosis, and DcR1, a decoy receptor that lacks a cytoplasmic tail and inhibits Apo2L function [3-5]. By cross-hybridization with DcR1, we have identified a fourth Apo2L receptor, which contains a cytoplasmic region with a truncated death domain. We subsequently named this protein decoy receptor 2 (DcR2). The DcR2 gene mapped to human chromosome 8p21, as did the genes encoding DR4, DR5 and DcR1. A single DcR2 mRNA transcript showed a unique expression pattern in human tissues and was particularly abundant in fetal liver and adult testis. Upon overexpression, DcR2 did not activate apoptosis or nuclear factor-kappaB; however, it substantially reduced cellular sensitivity to Apo2L-induced apoptosis. These results suggest that DcR2 functions as an inhibitory Apo2L receptor.

PMID: 9382840 [PubMed - indexed for MEDLINE]

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